REMARKS

Claim 1 has been amended. Claims 1-10 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Priority

The specification has been amended to recite priority to JP 2000-021842, filed January 26, 2000. Priority to this application under 35 U.S.C. § 119 has been claimed in the transmittal submitted upon filing of the application and in the Declaration & Power of Attorney submitted on April 9, 2001.

Rejection under 35 U.S.C. § 103(a)

Claims 1-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ford, et al. (6,472,173) in view of Schellenberg, et al. (5,449,604), Christian et al. (6,432,650) and Szyf, et al. (6,054,439) and further in view of Fodor, et al. (5,800,992).

It is not clear from the present record if the Examiner considers that Claims 9 and 10 are in condition for allowance.

The Examiner asserts that Ford, et al. teach the first two steps of claim 1 and that while Ford, et al. do not teach the third step of rubbing or shaving off the immobilized portions, the prior art is replete with means for collecting and transferring nucleic acids from one medium to another. The secondary references are cited to show such means.

Claim 1 has been amended to clarify that the single-stranded nucleic acids are immobilized via a covalent bond. Support for this amendment is found on page 7, paragraph 2, especially lines 9-11 of paragraph 2. The foremost issue is whether or not it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to collect hybridized nucleic acids by rubbing off or shaving off the immobilized portions when the immobilized nucleic acids are immobilized via a covalent bond. Applicant asserts that the invention as claimed is neither taught nor suggested by the combination of cited references, taken alone or in combination.

In the substrate of the present invention, the single-stranded nucleic acids are immobilized via a covalent bond. As a result, hybridized nucleic acids are also immobilized via

the covalent bond and an ion bond (due to the hybridization). Thus, in the substrate of the present invention, the nucleic acids are firmly immobilized.

The cited references do not teach all of the elements of the presently claimed invention

To Applicant's knowledge, while rubbing off or shaving off of nucleic acids from a substrate upon which the nucleic acids have not been firmly immobilized (that is, immobilization is by physical adsorption) was known, rubbing off or shaving off of nucleic acids from a substrate in which the nucleic acids are firmly immobilized (i.e. by covalent bond) was not known at the time of the claimed invention. None of the cited references teach or suggest rubbing off or shaving off nucleic acids which have been immobilized to a substrate via a covalent bond as presently claimed.

Schellenberg, et al. teach collecting the DNA of a selected chromosomal band region by scraping from karyotyped DNA. The chromosomal band region is obtained by fixing cells grown on coverslips and air-drying them (see col. 37. lines 5-12). The chromosomal band region thus obtained is immobilized only by physical absorption.

Christian, et al. teach collecting DNA regions of interest from metaphase chromosome spreads by scratching them off the coverslip carrying the spread. The spreads are obtained by dropping fixed cells on a solid surface and air-drying them (col. 6, lines 20-24). The spreads thus obtained are immobilized only by physical adsorption.

Szyf, et al. teach scraping nucleic acid spots from an array of spots on a thin layer chromatography plate. In thin layer chromatography, it was well known at the time of the claimed invention that the spots are not immobilized by a covalent bond on the plate.

Thus, none of Schellenberg, et al., Christian, et al., or Szyf, et al. teach collecting nucleic acids where the immobilized portion of the nucleic acid has been immobilized by a covalent bond.

Regarding Ford, et al. the Examiner admits that Ford, et al. differ from the third step of the claimed invention in teaching excision of nucleic acid spots from dried membrane filters rather than removal by "rubbing off" or "shaving off". Excision is clearly different from "rubbing off" and/or "shaving off" immobilized portions as recognized by the Examiner.

Fodor, et al. merely disclose a substrate having a plate shape.

Therefore, the combination of references does not teach or suggest all of the claim limitations. That is, none of the cited references teach or suggest collecting the immobilized

portions of hybridized nucleic acids by "rubbing off" or "shaving off" the immobilized portions when the single-stranded nucleic acids are immobilized to the substrate by a covalent bond. Consequently, it was totally unexpected at the time of the claimed invention that hybridized nucleic acids, covalently bound to a substrate, could be released by rubbing or shaving off the immobilized portions.

Advantages of the claimed invention satisfy a long-felt need

By applying "rubbing off" or "shaving off" to collect nucleic acids from an array (the substrate upon which the single-stranded nucleic acids are each separately immobilized), the following advantages are obtained.

While collection of nucleic acids by hybridization using a column in which nucleic acids are immobilized was known (e.g., an affinity column such as an oligo-T column), an array has a much smaller surface area per nucleic acid compared with a column. Consequently, collection in a liquid phase, while appropriate for a column is not appropriate for an array. In the case of a column, nucleic acids may be denatured in order to facilitate collection because the column has a larger surface area. However, it is difficult to collect nucleic acids from an array in a liquid system because the amount of the hybridized nucleic acid per dot is relatively small. Generally, the collected amount is sufficient only for detection by a method with high sensitivity such as scintillation counting (see col. 42, lines 51-56 of Ford, et al). This is also supported by the description of Cantor, et al. (U.S. Patent No. 6,007,987) which was cited in the previous Office Action. Cantor, et al. describe a complicated system for collection from an array (see Cantor, et al., col. 21, lines 42-49).

The presently claimed invention fulfills a long-felt need for a simple collection method from an array. By "rubbing off" or "shaving off" according to the presently claimed invention, immobilized nucleic acids may be collected at high concentration and in sufficient amount.

In the case of a gene, the presence of variants, different family members, alternate motifs and the like is expected and diverse kinds of hybrids may be present within one spot on the array. By the practice of the presently claimed method, isolation of the hybrids in sufficient quantities may be achieved. Thus, the presently claimed method has the advantage that sufficient quantities may be isolated such that it is not necessary to use PCR, real-time PCR, and the like in order to obtain sufficient product so that the species on the array may be identified.

Additionally, an array has several hundreds to several ten thousands of spots. Genes of several hundreds to several ten thousands can be separated in a location-specific manner. However, the use of a conventional affinity chromatography column in order to isolate and identify the spots necessitates high costs, complicated procedures and large amounts of each sample. The method of the presently claimed invention is efficient and allows low cost and simple procedures.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Jan. 14, 2004

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